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PRIEBE, SCOTT DAVID	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/206,040	BYRUM ET AL.	
	Examiner	Art Unit	
	Scott D. Priebe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 2* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *28* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed Oct. 6, 2003 has been entered. Claims 1 and 2 have been amended, and claim 3 has been cancelled in response to comments made by the Board of Appeals in the decision of Aug. 20, 2003 affirming the rejection of claims 1-3 under 35 USC § 101 & 112, first para. with new grounds of rejection under 37 CFR § 1.196(b). The amendment of claims 1 and 2 is deemed to resolve the issues of ambiguity raised in the Decision at pages 9-12.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The amendment filed Sept. 13, 2000 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the material inserted into the original specification at page 18, line 18, relating to a clone LIB3049-003-Q1-E1-H7, later designated ATCC No. PTA-2416, and the statement that SEQ ID NO: 1 is the sequence of the deposited clone. Applicant indicates that support for the amendment is found at page 18, line 18, which refers to a cDNA library designated LIB3049. The paragraph bridging pages 17 and 18 of the original specification refers to various embodiments of the invention relating to SEQ ID NO: 1. The last sentence of the paragraph describes an additional embodiment of one or more nucleic acid molecules which are 100% identical to nucleic acid molecules present in the LIB3049 library. Nowhere in this paragraph is any connection made between the source of SEQ ID NO: 1 and the LIB3049 library, i.e. it neither indicates that a clone of the library was used to determine

SEQ ID NO: 1, nor that any clone of the library comprised a nucleic acid whose sequence is SEQ ID NO: 1.

Examples 1 and 2 of the original specification describe how the LIB3049 library was made. The only information on the composition of the various nucleic acid molecules present in the library refer to the specific vector backbone used, an adapter used to ligate cDNA into the vector, and that the source of the cDNA inserted into the vector was young seeds from young soybean pods. The Examples do not mention SEQ ID NO: 1 or any specific clone.

The La Rosa Declaration filed Sept. 13, 2000 states that SEQ ID NO: 1 "was derived from a soybean clone designated "LIB3049-003-Q1-E1-H7"". It does not state that this clone was present in the library LIB3049 described in the specification, nor does the specification describe LIB3049-003-Q1-E1-H7. The La Rosa declaration also does not state that SEQ ID NO: 1 was the sequence of this undisclosed clone, or that the clone contained a nucleic acid molecule comprising SEQ ID NO: 1. If in fact LIB3049-003-Q1-E1-H7 was present in the LIB3049 described in the original specification, then it is apparent from Example 1 that SEQ ID NO: 1 cannot be its sequence, since the clone presumably would contain a nucleic acid molecule comprising pSPORT and adapter sequence in addition to a cDNA insert. SEQ ID NO: 1 does not include the sequence of pSPORT. That SEQ ID NO: 1 was "derived from" LIB3049-003-Q1-E1-H7 does not necessarily mean that LIB3049-003-Q1-E1-H7 contains SEQ ID NO: 1. The declaration does not make any assurance that the sequence (SEQ ID NO: 1 is identical to the corresponding cDNA present in the clone.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 101

Claims 1 and 2 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, for the reasons of record set forth in the decision (pages 13-32) of Appeal No. 2002-0078 on Aug. 20, 2003 by the Board of Appeals under 37 CFR 1.196(b), which is reproduced below but without the footnotes, and the Examiner's Answer of Aug. 6, 2001, which is repeated below except for modifications necessitated by the amendment of the claims.

Grounds of rejection set forth in the decision of Appeal No. 2002-0078 by the Board (reproduced below with footnotes omitted).

> "The starting point for determining whether a nucleic acid molecule having the 469 nucleotide sequence set forth in SEQ ID No. 1 possesses utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). The Court stated "the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point--where specific benefit exists in currently available form--there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695. In considering the issues presented in this appeal, special attention must be paid to the Court's statement that a patent should issue only when an invention possesses "substantial utility," i.e., "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C. § 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

> [i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—

there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid

derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a

characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. See id., 26 USPQ2d at 1606. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." Id., 26 USPQ2d at 1605.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that "[it] is axiomatic that an

invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by "marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds . . ., analogous to the benefit provided by the showing of an in vivo utility." Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that

little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best . . . on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

With these principles in mind we turn to the issues at hand. Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, i.e., identification and detection of polymorphisms and use as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 28-35 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification is not specific to the 469 nucleotide molecule depicted in SEQ ID No. 1. Nor does the specification explain why the 469 nucleotide molecule of SEQ ID No. 1 would in fact be useful in detecting polymorphisms. Rather, appellants' argument is that "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." Appeal Brief, page 14. In other words, appellants' position is that an EST by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage and can be viewed to be at the lower end of the utility spectrum. At the high end of the utility spectrum would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the EST is derived has in the development and/or phenotype of the

plant. Somewhere between having no knowledge of the gene and its role in the plant's development and phenotype (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.

Dr. Wiegand's declaration does not aid appellants in this aspect of their case. Polymorphism as a utility is discussed primarily in paragraphs 20-23 of the declaration. Two probes were used in Dr. Wiegand's work, "a synthesized nucleic acid molecule based on overlapping oligomers matching SEQ ID No. 1; and a probe derived from the plasmid that carries clone LIB3049-003-Q1-E1-H7, from which SEQ ID No. 1 was determined." Dr. Wiegand concludes that "a nucleic acid molecule having a sequence of SEQ ID No. 1 can be synthesized and successfully used to detect polymorphisms in soybean chromosomal DNA. Accordingly, a nucleic acid molecule having the sequence of SEQ ID NO. 1 is useful for detecting polymorphisms in order to develop a genetic map, determining if a plant carries the gene for a particular trait, determining the copy number of a particular gene in a plant, or for other purposes."

First, the precise identity of the nucleic acid molecules used in Dr. Wiegand's work is unclear. As stated above, we are limiting our consideration of the issues raised in this appeal as they pertain to the precise 469 nucleotide molecule set forth in SEQ ID No. 1. Dr. Wiegand's conclusions are premised upon use of "a nucleic acid molecule having the sequence of SEQ ID No. 1." It is unclear whether the probes used contained only the specific 469 nucleotides depicted in SEQ ID No. 1 or contained additional nucleotides before and/or after the specific 469 nucleotide molecule set forth in SEQ ID No. 1.

In any case, it is not clear how the results reported in the declaration establish a substantial utility. Dr. Wiegand does not state in his declaration that these results provide any significant knowledge. To the contrary, they appear to represent what one might reasonably assume--a given EST may or may not detect a polymorphism in a related organism. While such knowledge may indicate the molecule is "useful" to some degree, we do not find that it represents a substantial utility.

b. Probes or source of primers

Appellants argue that the specification "discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...." Appeal Brief, page 16. While that may be true, it begs the question of what substantial use such knowledge would have? Again, the present specification does not attribute any property in terms of plant trait, or phenotype to the 469 nucleotide molecule of SEQ ID No. 1. Why does knowledge that a similar molecule may exist in another organism represent a substantial utility?

The same analysis holds for the stated utility that a nucleic acid molecule may be used in a "chromosome walk." Id., pages 16-17. In presenting this argument, appellants run afoul of the confusion engendered as to the source of the present nucleic acid molecules. Appellants' argument at page 17 of the Appeal Brief is couched in terms of the ability to isolate a promoter that is active in young seed pods (5 to 15 days after flowering). It appears that this argument is premised upon the fact that the nucleic acid molecule of the present invention was obtained from young seed pods. However, as explained above, the examples of the specification state that the nucleic acid molecule was obtained from young seeds collected from young pods.

Appellants state that the examiner denigrated the "chromosome walk" utility by stating in the Final Rejection that "[a]ny nucleic acid molecule from any plant cell

generally serves this purpose...." Appeal Brief, page 16. Appellants argue in essence that despite the fact that the argued utility applies to all ESTs, there is no legal requirement that an invention's utility be "unique" to the invention, i.e., an invention can be a member of a class, where all the members of the class share a common utility.

First, appellants have only been required to identify a utility that is specific to the invention claimed. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695 (An invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form.). An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

Nor does Dr. Wiegand's declaration assist appellants in this portion of their position on appeal. Dr. Wiegand discusses the use of EST's to generate probes in paragraphs 14-17 of his declaration. However, that work is based upon a synthetic probe stated to be "a true enough copy of SEQ ID No. 1." It is not apparent why evidence

based upon "a true enough copy" of SEQ ID No. 1 is relevant in this appeal.

c. Other Arguments

Appellants argue that the specification describes other utilities for the claimed nucleic acid molecules including "introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Appeal Brief, page 10. Specifically, appellants argue that a compound can be provided to both an antisense plant and a control plant not having antisense, with the effect of the compound on the plant being monitored. Appellants analogize this proposed procedure to a "cell-based assay" which appellants assert to have a "legally sufficient utility." Id.

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. The portion of the specification cited in support of this argument (page 64) indicates that the nucleic acid molecule must be introduced into a plant cell and transcribed using an appropriate promoter to result in the co-suppression of an endogenous protein. The specification does not indicate that such a method is feasible when the nucleic acid to be used is uncharacterized as here. Such a use does not provide a specific or substantial benefit in currently available form.

Appellants also argue that the claimed nucleic acids are useful to measure the level of mRNA in a sample through use of microarray technology and use as molecular markers. Appeal Brief, pages 10-11. In regard to microarrays, appellants argue that it is "standard practice" to screen populations of nucleic acids with EST sequences without characterizing each and every target mRNA. Reference to para. 14 of the Wiegand declaration is made in support. Appeal Brief, page 11, n. 5. Dr Wiegand states "Soybean DNA clones are routinely used to detect expression levels of corresponding naturally occurring soybean nucleic acids. A nucleic acid molecule of SEQ ID NO: 1 can also

certainly be used to detect expression level. Use of a nucleic acid molecule representing an EST as an expression probe is a practical use because it enables the detection of changes in expression of a particular gene." Wiegand decl., para. 14.

We find that the asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form.

We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid depicted in SEQ ID NO: 1. However, the specification provides no guidance which would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the SEQ ID NO: 1-specific information derived from a gene expression experiment would mean.

Suppose, for example, that a researcher found that SEQ ID NO: 1 expression was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in SEQ ID NO: 1 expression would depend on other factors, but again the specification provides no hint what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using SEQ ID NO: 1 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure

provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use SEQ ID NO: 1-specific gene expression data.

Here, appellants assert that SEQ ID NO: 1, along with every other expressed soybean gene or protein, or for that matter, any expressed gene or protein, can be used to monitor changes in gene expression. However, without additional information, any observed results of changed expression of SEQ ID NO: 1 would have no meaning. The specification in effect discloses that the claimed nucleic acids can be used to monitor gene expression, and those of skill in the art will figure out what to do with the gene expression data. This utility is not substantial; it does not provide a specific benefit in currently available form.

Assuming arguendo that a generic gene expression assay—one based on monitoring expression of thousands of uncharacterized nucleic acids would provide a useful tool for, e.g., drug discovery, it does not follow that each one of the nucleic acids represented in the assay individually has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid—its data point—is only a tiny contribution to the overall picture.

The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard. The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants assertion that the nucleic acid depicted in SEQ ID NO: 1 is useful as a molecular marker or probe. It is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of SEQ ID NO: 1 as a molecular marker or probe represents a substantial use.

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Appeal Brief, pages 19-21. Reliance is placed on paragraph 6 of the Wiegand declaration in support of this argument. Dr. Wiegand statements in this paragraph of his declaration refer to EST databases, clone sets and microarrays. Suffice it to say, the claims on appeal

are not directed to EST databases, clone sets and/or microarrays. Again, it is not seen that the one data point which may be provided by using the uncharacterized nucleic acid of SEQ ID NO: 1 in such devices represents a substantial use."

Additional basis for the rejection under 35 USC § 101as expressed in the original grounds of rejection.

The invention is drawn to nucleic acid molecules either consisting of or comprising the nucleotide sequence as set forth in SEQ ID NO: 1 or the complete complement of SEQ ID NO: 1. The nucleic acid molecule set forth as SEQ ID NO: 1 is an expressed sequence tag, or EST, made as a partial cDNA from an mRNA isolated from a young seed pod (5 to 15 days post-flowering) from *Glycine max* (soybean) cultivar Asgrow 3244. In the art, an EST is a tag or molecular marker for a corresponding mRNA that contains it and for the corresponding gene which expresses that mRNA. The utilities disclosed for the EST of SEQ ID NO: 1 or fragment thereof, or a nucleic acid molecule comprising same, or a complete complement of these, are:

- Use the EST as a probe for screening to identify sequence polymorphisms linked to the sequences corresponding to the claimed nucleic acid molecule in a genome, and then use as a probe for detecting the polymorphisms, which serve as a molecular marker, either a) for a mutation affecting the expression of a product encoded, at least in part, by the claimed nucleic acid molecule (specification, pages 27-28) or b) for a desirable trait that is genetically linked to the polymorphism (specification, pages 35-36);

-Use of the EST as a probe for detecting a physical map location, e.g. as a marker in *in situ* hybridization;

-Use as a probe or source of PCR primers either to isolate other nucleic acid molecules (e.g. complete cDNA, protein coding sequence, genomic fragment, promoter, start of a chromosome walk) from the same organism or different organisms, i.e. other plants, or to detect other nucleic acid molecules (e.g. mRNA, chromosomal region, chromosome). Disclosed for the latter, for example, is to detect the mRNA in different tissues or as a measure of protein expression from the mRNA (based on mRNA levels), particularly if there is a mutation (hypothetical) affecting expression;

-Use of the EST as an antisense inhibitor of the corresponding mRNA; and

-Use as a probe to identify or isolate proteins that might bind to the EST sequence.

Each of these utilities requires additional knowledge about the EST before the EST can be used for a specific purpose, such as: whether there are in fact sequence polymorphisms linked to the gene corresponding to the EST and, if so, their identity; the map location of the corresponding gene; the sequence of the corresponding complete mRNA sequence, protein coding sequence or genomic sequence; the function of the protein encoded by the corresponding mRNA; the identity and phenotype, if any, of a mutation in the corresponding gene; the tissue distribution of the corresponding mRNA and tissue-specific expression levels; *etc.* The specification does not provide any such information specific to the disclosed EST. Consequently, the disclosed utilities are *non-specific* utilities, since any of the general disclosed utilities would apply equally to any uncharacterized nucleic acid molecule from soybean in particular, or plants or other organisms in general. Moreover, since practice of these utilities would first require research on the disclosed EST itself, i.e. there is no apparent *immediate* benefit to the public, the disclosed uses are not substantial. The only readily apparent

immediate use for the disclosed EST is as an object of further scientific inquiry aimed at characterization of the EST itself in terms of identity of corresponding sequence polymorphisms (if any), map location, sequence and function of the corresponding mRNA and polypeptide, tissue distribution of the corresponding mRNA and polypeptide, *etc.* These *immediate* uses are merely searches for a specific and substantial statutory utility for the claimed invention that fail to meet the statutory utility requirement. In *Brenner v. Manson*, 148 USPQ 689, 696 (US, 1966), the Court held that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." The original disclosure lacks any successful conclusion for even one of the vague and general utilities disclosed. Thus, no "substantial" or "real world" utility has been disclosed.

Further, there is no evidence of a well-established utility for the disclosed EST or claimed nucleic acid molecules.

Claim Rejections - 35 USC § 112 (Enablement)

Claims 1 and 2 remain also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In addition, claim 1 contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most

nearly connected, to make the invention as directed to nucleic acid molecules comprising the EST of SEQ ID NO: 1, or its complete complement, and additional nucleotide sequences linked to the EST.

The following grounds of rejection are essentially the same grounds set forth in the Examiner's Answer of Aug. 6, 2001. To address the Board's concerns, headings have been added to identify where various factors discussed in *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) are addressed in the instant rejection.

Breadth of the claimed invention and nature of the invention

The claims are not enabled because the specification fails to teach one of skill in the art how to use the claimed nucleic acid molecules commensurate in scope with the claim, such that one of skill in the art could identify a target nucleic acid without undue experimentation. All of the utilities disclosed for the claimed nucleic acid molecules require hybridization to some target nucleic acid, in some capacity. Claim 1 embraces an essentially infinite genus of nucleic acid molecules comprising SEQ ID NO: 1 even when just considering nucleic acid sequences and ignoring nucleic acid molecules comprising non-nucleotide moieties. The specification does not explicitly disclose any nucleic acid molecules that "comprise" SEQ ID NO: 1, other than SEQ ID NO: 1 itself, either unlabeled or labeled with a detectable non-nucleotide moiety such as a fluorophor. No other specific nucleic acid molecules are disclosed wherein the nucleic acid sequence is extended beyond contiguous nucleotides present in SEQ ID NO: 1, except for a general teaching of incorporating ESTs into vectors. As indicated above, the original specification did not describe a cloned nucleic acid molecule from which SEQ ID NO: 1 was determined.

Lack of sufficient guidance and working examples in the specification.

The specification does not teach the content of or the maximum length or location (5' end, 3' end, or both ends) of nucleic acid sequence(s) that could be added to SEQ ID NO: 1, that would not interfere with its disclosed use as a hybridization probe. The specification provides no guidance whatsoever other than labeling a nucleic acid molecule "consisting of" SEQ ID NO: 1 or an oligonucleotide fragment of SEQ ID NO: 1. The only working example demonstrates using a cloned EST nucleic acid molecule as a template for PCR sequencing, i.e. experimentation on the claimed invention.

Unpredictability and quantity of experimentation

Without knowing the composition of the target DNA, such as the size of a corresponding mRNA, the size of a specific genomic DNA, restriction endonuclease fragment or amplified fragment, or the extraneous sequences that may be added to the probe or primer, one would be unable to predict whether the probe or primer would function as expected under any given reaction conditions to hybridize or amplify a specific nucleic acid molecule corresponding to the intended target. Since the claims embrace adding any and all nucleic acid sequences to the core nucleic acid molecule of SEQ ID NO: 1, one cannot predict whether or not the additional nucleic acid sequence added would hybridize to a target nucleic acid molecule other than the intended target nucleic acid molecule. When such a situation occurs, and more than one nucleic acid molecule is amplified or detected in hybridization, the skilled artisan would have no information that would allow the desired target nucleic acid molecule to be distinguished from a nucleic acid molecule that was targeted by the added nucleic acid sequences. This simple situation would be further complicated if SEQ ID NO: 1 or the

intended target nucleic acid were one of a number of different repeated nucleotide sequences in a sample or if the added nucleotide sequence comprised one of a number of different repeated nucleic acid sequences in a sample, each with varying degrees of binding specificity under hybridization or amplification reaction conditions between primer or probe and target nucleic acid molecules. Foster-Harnett et al. (Genome 45: 634-645, 2002, provided by Applicant with the Information Disclosure Statement of Oct. 6, 2003) discloses that low-copy sequences in the soybean genome were known to be repeated two or more times (p. 643). One cannot predict whether either the intended target nucleic acid or nucleic acid sequences added to a probe or primer are one of a number of repeated nucleic acid sequences; trial and error experimentation would be required.

Consequently, making the astronomically large myriad of nucleic acid molecules embraced by the claims and testing the suitability of each for use as a probe or primer for the disclosed utilities in the absence of guidance or examples would require excessive trial and error experimentation due to the unpredictability involved, and would therefore require undue experimentation.

Claim Rejections - 35 USC § 112 (Written Description)

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The original rejection is withdrawn in light of the new grounds of rejection set forth below, which expands upon the original rejection by

incorporating material previously presented by the Examiner only in response to Applicant's arguments, but not presented formally as part of the original rejection.

The Board had not reached this rejection in its decision, and suggested that the Examiner take into account "Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first para. Written Description Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001), hereafter the "Written Description Guidelines" and *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). The examiner has done so in formulating the following rejection.

The essential goal of the written description requirement is to clearly convey information that the applicant invented and possessed the subject matter being claimed. Applicant may show possession of a generic invention by describing it with all of its limitations using descriptive words, drawings, or formulas sufficiently detailed to show that applicant possessed the claimed invention as a whole, or by disclosing sufficiently detailed, relevant identifying characteristics such as with complete or partial structures, physical or chemical properties, and functional characteristics with a known or disclosed relationship between structure and function, or by disclosure of a representative number of species. A suitable deposit of biological material will satisfy written description for the material deposited. (See for example, the Written Description Guidelines at sections I. & II.3.a., *Enzo* at 1613-1614). However, it has not been settled whether a biological deposit of nucleic acid may satisfy the written description requirement for a broader invention embracing it. In *Enzo*, the court determined that the deposit of 3 sequences did not necessarily provide an adequate written description for claims directed to the three deposited sequences and subsequences and mutated

variations thereof. *Enzo* at 1614-15. In the present case, the description of SEQ ID NO: 1 does not provide adequate written description for the breadth of the invention claimed. While the specification need not describe every nuance of the claimed invention, the written description must bear reasonable correlation to that which is claimed.

Claim 1 is drawn to nucleic acid molecules "comprising" the EST of SEQ ID NO: 1 (or the complete complement thereof). By "complete complement" of SEQ ID NO: 1, one of skill in this art would understand that the "complement" is the same length as SEQ ID NO: 1, and contains a complementary nucleotide for every nucleotide of SEQ ID NO: 1 (i.e., A for T or U, T or U for A, G for C, C for G) and could form an antiparallel homoduplex with a nucleic acid molecule whose sequence is SEQ ID NO: 1.

The claim permits the nucleic acid molecule to contain the nucleotide sequence of SEQ ID NO: 1 (or the complete complement thereof), and any number or type of non-nucleotide moieties or any number or type of additional nucleotides. The claim permits the nucleic acid molecule to comprise additional moieties or nucleotide sequences that are conventionally attached to nucleic acid molecules, such as detectable labels where used in hybridization, vectors for use in isolating and producing the nucleic acid molecules, linker or adapter oligonucleotides for use in constructing vectors containing the nucleic acid molecules, and moieties required for chemical synthesis of nucleic acid molecules. The specification does not disclose actual reduction to practice of any nucleic acid molecules that "comprise" SEQ ID NO: 1, other than that of a nucleic acid molecule consisting of SEQ ID NO: 1. The specification as amended on Sept. 13, 2000 (at page 18) includes a description of a deposited DNA clone comprising SEQ ID NO: 1. However the description of this clone added to the

specification is not supported by the original specification for the reasons set forth above in the objection to the specification. Consequently, this deposit does not constitute part of the written description of the claimed nucleic acid molecules in the specification as filed.

The specification constructively describes nucleic acid molecules consisting of SEQ ID NO: 1 and non-nucleotide labels such as a fluorophor, and nucleic acid molecules comprising a vector and a cDNA insert consisting of SEQ ID NO: 1. It is acknowledged that the specification need not disclose specific structures of additional moieties, such as labels or vectors, which are conventionally added to nucleic acid sequences.

However, the claim is not limited to nucleic acid molecules comprising conventional additions to SEQ ID NO: 1. The actual reduction to practice of a single species, a nucleic acid molecule consisting of SEQ ID NO: 1, is not representative of the genus being claimed. Furthermore, even assuming *arguendo* that the description of a deposited DNA clone comprising SEQ ID NO: 1 (objected to as new matter, *supra*) could be relied upon by applicant as evidence of a second species, the deposited clone does not appear to be representative of the genus being claimed.

First and foremost, the claim permits additional nucleotide sequences that would be adjacent to the disclosed EST in mRNA or genomic DNA present in soybean, or in complete or partial cDNA copies of mRNA isolated from soybean that extend beyond SEQ ID NO: 1. The Written Description Guidelines (section I.A., with reference to footnote 13) direct the Examiner to determine whether originally claimed nucleic acid molecules that necessarily embrace nucleic acid molecules comprising non-conventional, specific structures such as coding regions or regulatory elements found in corresponding genes, are adequately described

in the specification. The instant specification does not provide any structural or functional characteristics for these additional structures. Nor is there any known or disclosed structural relationship between one nucleotide sequence and another nucleotide sequence to which it is linked in nature. To the extent that the claim embraces nucleic acid molecules which comprise specific nucleotides associated with or linked to SEQ ID NO: 1 in soybean, the specification fails to disclose or describe them.

A disclosed functional characteristic, of some but not all claimed nucleic acid molecules, is that the nucleic acid molecule encode a protein corresponding to a protein encoded by the gene found in soybean corresponding to SEQ ID NO: 1 (e.g. specification, pages 10-11, 19-21). Examples of such nucleic acid molecules would be a complete mRNA (or cDNA) or genomic DNA from soybean corresponding to SEQ ID NO: 1. The specification does not indicate that SEQ ID NO: 1 itself contains any sequence encoding a protein, nor does it identify any protein that could be encoded by nucleic acid molecules comprising SEQ ID NO: 1 and found in soybean. The court and the Board have repeatedly held (*Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (CA FC, 1991); *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993); *Fiddes v. Baird*, 30 USPQ2d 1481 (BPAI 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)) that an adequate written description of a nucleic acid requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, irrespective of the complexity or simplicity of the method; what is required is a description of the nucleic acid itself. Unlike the situations in these cases, the instant specification provides no distinguishing structural or functional characteristics for the hypothetical protein encoded by some of the

claimed nucleic acid molecules, much less for the claimed nucleic acid molecules which encode such a protein. Consequently, the specification fails to provide evidence that Applicant possessed this subgenus of the claimed invention, and clearly fails to provide a description adequate to inform the public.

Second, the claim permits additional heterologous nucleotide sequences that would not conventionally be attached to a nucleic acid molecule to be used as a probe, or in construction of a vector, for example. Thus, the claim is directed to an astronomically large genus of nucleic acid molecules comprising SEQ ID NO: 1 when solely considering nucleic acid sequences and ignoring nucleic acid molecules comprising non-nucleotide moieties such as detectable labels.

The only disclosed functional characteristic of all nucleic acid molecules embraced by the claim is that they hybridize to a target nucleic acid molecule found in soybean, e.g. mRNA or genomic DNA. This property is inherent in the structure of SEQ ID NO: 1 itself. Nearly all of the potential utilities described in the specification involve using the claimed nucleic acid in hybridization either directly as in the case of detecting polymorphisms or as anti-sense inhibitors, or indirectly as in the case of isolating nucleic acids encoding the protein of the soybean gene corresponding to SEQ ID NO: 1. It is conventional in the hybridization art to use vectors containing probe sequences or probe sequences comprising short nucleotide sequences, e.g. adapters or capture probes for signal amplification, and the specification need not describe such conventional additions with particularity. However, it is not conventional in the hybridization art to arbitrarily attach additional nucleotides. One reason for this, is to avoid the possibility of such arbitrary nucleotide sequences hybridizing to nucleic acids in a sample

that are not the desired target of the probe. For example, the specification does not contain a working example of using the claimed nucleic acid molecules in any method involving hybridization, such as detection of genomic DNA fragments comprising all or part of SEQ ID NO: 1. If one were to carry out a hybridization with a probe comprising SEQ ID NO: 1 and an arbitrary additional 1 kilobase sequence against a series of restriction endonuclease digests of soybean genomic DNA, and detected hybridization of the probe to multiple fragments in each case, one would not know whether hybridization to all fragments was mediated by SEQ ID NO: 1 or whether hybridization to some fragments was mediated by the arbitrary sequence. If the latter, one would not know which fragments hybridized to SEQ ID NO: 1 and which to the arbitrary sequence. One would be able to envision the structure of additional sequences that would not hybridize with soybean genomic DNA only if the complete sequence of the soybean genome was available for comparison. However, there is no evidence of record that the soybean genome sequence was known at the time the application was filed, and the instant specification does not disclose it. Thus, the instant specification does not adequately describe additional sequences that may or may not be added to SEQ ID NO: 1, which would not interfere or interfere, respectively, with the disclosed use of the claimed nucleic acids in hybridization.

Response to Arguments

Applicant's arguments filed October 6, 2003 have been fully considered but they are not persuasive.

Response to Section I. & IIA., of Applicant's reply.

The specification alludes to various different potential utilities for the claimed nucleic acid molecules, including utilities that require using the claimed nucleic acid molecules: as a probe for the detection of polymorphisms; as a probe for isolating nucleic acid molecules from soybean, e.g. complete mRNA or genomic sequence, a linked promoter, etc., or from other plants; as a sense or antisense inhibitor of gene function; and as a probe for measuring mRNA levels or expression patterns. The original rejection and the new grounds of rejection set forth in the Board Decision address all of the potential utilities alluded to in the specification. However, Applicant's response to the Board Decision addresses only one of these classes of utility, specifically where the claimed nucleic acid molecules are used to detect polymorphisms.

Applicant (p. 4) takes issue with the analogy made by the Board in its decision (pp. 22-23) referring to "utility" of an EST from a plant as a "spectrum," with insubstantial uses at one end and substantial uses at the other end, and at some point in between "lies the line between "utility" and "substantial utility"" (Decision, p. 23). Applicant argues that the analysis is improper. In response, the Board's choice of language is not at issue here. The question is only whether the specification describes at least one specific and substantial utility for the claimed nucleic acid molecules. (No evidence or argument has been presented for at least one undisclosed, well-established utility for the claimed nucleic acid molecules that would have been readily apparent to one of skill in the art at the time the application was filed on Dec. 4, 1998.) The Board clearly held that the claimed invention lacked substantial utility, and explained the basis for their decision. While the bar for meeting the utility requirement under

§101 is not high, the claimed invention fails to meet that bar, regardless of how one chooses to describe the utility requirement. The credibility of the alleged utilities is not at issue, since it is accepted that the claimed nucleic acid molecules would hybridize at least to nucleic acids corresponding to SEQ ID NO: 1 present in domestic soybean, *Glycine max*. Rather, the issue is whether the specification disclosed any specific and substantial use in carrying out such a method using the claimed nucleic acid molecules with nucleic acids from *G. max* or any other plant species.

The reply (p. 7) re-iterates the assertion that the claimed nucleic acid molecules are useful for determining the presence or absence of a polymorphism in a plant population, particularly a soybean population. The response refers to where the specification teaches this generally, and where the Brief discusses the assertion. General statements are made concerning the general usefulness of polymorphisms for analyzing whether a plant contains a mutation affecting the pattern or expression of mRNA in the plant, and for mapping important agronomic traits, referring to ¶20 of the Wiegand Declaration. The reply then jumps to the conclusion, based upon these assertions, that the claimed invention provides a known, currently available benefit (presumably to the public in a "real world" context of use). In footnote 2, applicant asserts that this "utility" was well characterized and confirmed by the Wiegand Declaration.

Applicant further argues (Reply, p. 8) that ESTs are commonly used as molecular markers, and that molecular markers are used in genetic mapping for a variety of practical purposes, as stated in the Wiegand Declaration (¶ 12). Applicant cites Foster-Harnett et al. and Liebhard et al. purportedly to show that the utility of EST molecules is well recognized in the

art for these purposes, and then equates the use of the claimed EST with the situation in *Nelson v. Bowler*, 206 USPQ 881, 883 (CCPA 1980).

In response, the insufficiency of this argument has been thoroughly addressed in the Examiner's Answer (p. 23-24, 26-36, 41-43) and in the Board Decision (p. 22-24). An application must meet the utility requirement as of its filing date. *In re Wright*, 27 USPQ2d, 1510, 1514 (Fed. Cir. 1993). The specification (pages 27-29, particularly at page 28, full para. 4 to the para. bridging pages 28-29) describes various general uses of polymorphisms, but fails to provide any specific information for how the claimed nucleic acid molecules can be used for these purposes. As defined in the specification, "a "polymorphism" is a variation or difference in the sequence of the gene or its flanking regions that arises in some of the members of a species" (emphasis added). To summarize the reasons set forth in the Examiner's Answer why the original specification fails to disclose a specific and substantial utility for the claimed nucleic acid molecules in the context of detecting polymorphisms, and the use of detecting polymorphisms as part of a practical application:

- the specification fails to disclose whether, in fact, there is a polymorphism that can be detected with the claimed nucleic acid molecule (consisting of or comprising the nucleotide sequence of SEQ ID NO: 1);
- if there is no such polymorphism, the specification fails to assert a use for the claimed nucleic acid molecules in this context;
- even if there were a such a polymorphism, the specification fails to identify it, i.e. either the inventors did not know or failed to disclose it;

- even if there were a such a polymorphism, the specification fails to disclose any trait conferred by a mutation in the gene corresponding to the claimed nucleic acid molecule for which the polymorphism would serve as a molecular or genetic marker; and
- even if there were a such a polymorphism, the specification fails to disclose any desirable or undesirable trait for which the polymorphism could be used as a molecular or genetic marker.

Applicant has never disputed that the specification fails to disclose this information. The Board summarized the deficiency of the specification indicating that the specification provides no explanation as to why a nucleic acid molecule consisting of SEQ ID NO: 1, specifically, would be useful in detecting polymorphisms, and that the Wiegand Declaration does not indicate how the results provided any significant knowledge.

Since experimentation would be required to determine whether, in fact, a polymorphism existed that could be detected with the claimed nucleic acid molecules, and if it existed, how it specifically could be used for the benefit of the public, this use was not "currently available" in a "real world" context at the time the application was filed. Therefore, the specification fails to disclose a substantial utility for the claimed invention in this context. Since any EST can be used in a similar process of discovery, e.g. determining whether it can be used to detect a polymorphism, the specification fails to disclose a specific utility for the invention in this context.

With respect to the showing in the Wiegand Declaration, Wiegand used a probe purported to be a "true copy" of SEQ ID NO: 1 to detect genomic DNA isolated from each of two species of the genus *Glycine*, *G. soja* and *G. max* (from which the EST of SEQ ID NO: 1

was isolated). Wiegand determined that the probe detected restriction endonuclease fragments of different sizes between the two species (¶ 20-23), but does not report that any such variation was found between individuals of *G. max* (¶ 17-18). The latter results fails to support the existence of a polymorphism, as the term is defined in the specification, and thus any use requiring detection of polymorphisms. The former result is not relevant to the issue at hand, since genetic variation in nucleotide sequences between two different species of plant is not "polymorphism" as defined in the specification. *G. max* and *G. soja* are separate species. See National Center for Biotechnology Information, Taxonomy Browser, on the World Wide Web at ncbi.nlm.nih.gov/htbin-post/Taxonomy, and Ahmad et al. (J. Hered. 70: 358-364, 1979). Therefore, the example provided in the Wiegand Declaration of detecting sequence variation between species of a genus, *G. max* and *G. soja*, is not a utility disclosed in the specification, since polymorphism is defined in the specification as existing between some members of a species, not between different species of a biological genus. The court (*In re Kirk,* 153 USPQ 48 (CCPA 1967) has held that *ex post facto* asserting a utility that is not disclosed in the original specification and that is consistent with a vague and general disclosed use, amounts to "an admission that experimentation would be necessary to determine actual uses - or possible lack of uses – of the compounds, as well as how to employ them in a useful manner" (*Kirk* at p. 53), and the issue of whether claimed compounds "do *in fact* possess specific ... activity or usefulness" is not at issue, but rather it is "what the compounds are *disclosed* to do that is determinative" (*Kirk* at p. 52, emphasis in the original).

With respect to references allegedly cited on pages 11-12 of the reply filed Aug. 20, 2000, no references were cited. With respect to the references newly cited in Applicant's

October 6, 2003 reply, both were published well after the instant application was filed. An application must meet the utility requirement as of its filing date. *In re Wright*, 27 USPQ2d at 1514. Consequently, these references cannot be used to support Applicant's arguments. Furthermore, the only mention of ESTs made in Foster-Harnett et al. simply states that a large collection of soybean ESTs is available (p. 635, col. 2), and does not discuss how such ESTs are used or useful. Liebhard makes no mention of ESTs at all.

With respect to *Nelson v. Bowler,* this situation is not analogous to that in *Nelson* where the original *specification* (not an *ex post facto* affidavit) disclosed very specific pharmacological activities for the claimed compounds that the court deemed an adequate showing of practical utility. The court specifically contrasted the situation with that in *Rey-Bellet v. Englehardt*, 181 USPQ 453 (CCPA 1974) where the disclosed evidence for pharmacological activity was deemed inconclusive, and thus failed to prove practical utility. In both cases, the claimed compounds were structural analogs for prior art pharmacologic compounds with known specific uses. The utility issue turned on whether evidence disclosed in the specification was sufficient to establish pharmacological similarity as well. That is not the case here: the original specification does not disclose any specific use for the claimed nucleic acid molecules other than using them to identify a specific use, much less a known structural analog with a known specific use to which the claimed nucleic acid molecules can be compared.

Contrary to Applicant's assertion that the Examiner and the Board have sidestepped the issue, both have addressed the issue head-on, in the Examiner's Answer and the Decision respectively. Rather, the fundamental issue, regarding the asserted general use to detect

polymorphisms, is that the specification fails to disclose any information to reasonably assure one of skill in the art that the claimed nucleic acids could be used to detect a polymorphism or that a polymorphism even exists to be detected, and fails to disclose any specific and substantial use for identifying a polymorphism with the claimed invention as part of a practical use, e.g., as a marker for a specific desirable or undesirable trait. Consequently, the assertion that the claimed invention can be used to detect polymorphisms is a vague assertion of possible future utility, *vis a vis In re Ziegler*, or is so general as to be meaningless, *vis a vis In re Kirk.* The Court in *Brenner v. Manson*, 148 USPQ 689, 696 (US 1996) pointed out that products whose sole utility is as an object of further research to increase scientific knowledge do not meet the utility requirement under § 101. That is the case here, where further experimentation would have been required to first determine whether the claimed invention could even detect a polymorphism, and then, if it could, to determine how detecting the polymorphism could be used for a practical purpose, such as marking a linked desirable or undesirable trait. The claimed invention is useful to some degree, i.e., research in further characterizing it and its potential uses, but such use is not a substantial utility as required under § 101.

Response to Section IIB. of Applicant's reply

With respect to the additional grounds of rejection of claim 1 under 35 USC 112, first para. for lack of enablement commensurate in scope with the claims, Applicant incorporates the arguments made on pages 27-36 of the Brief filed Jan. 31, 2001. No new arguments have been provided. The arguments made in the Brief have been addressed in the Examiner's Answer filed Aug. 6, 2001 (pages 45-53), as reproduced below.

"I) Response to Brief Sections 8.D.(2), 8.D.(2)(a), 8.D.(2)(b).

Subsection (1) reprises the inseparable connection between patentable utility and the "how to use" requirement under 35 USC 112, first paragraph. Subsection (2) appears to question the propriety of rejecting claims 1 and 3 for not being commensurate in scope with the disclosure in terms of both how to make and how to use the invention. The Examiner maintains that the use asserted for the claimed invention are methods where the claimed invention is, itself, an object of scientific study, e.g. to determine the tissue distribution of corresponding mRNA embraced by the claims or to determine whether the corresponding genomic DNA of soybeans contains a polymorphism that can be detected with the claimed invention.

Appellants argue that the rejection is improper on its face because the rejection only refers to uses that involve hybridization, either as a probe or as a primer. This concern is not well taken, because all of the other speculative utilities disclosed in the specification employ hybridization at some point using claimed nucleic acid molecules. In order for a primer to work in an amplification reaction, such as PCR, it must hybridize at least transiently with its intended target sequence. Appellant misapprehends the reason for the additional grounds of rejection under 35 USC 112, first para. which was directed to reasons for lack of enablement in addition to that dictated by the failure of the specification to disclose a specific and substantial utility. Regardless of whether the specification teaches a specific and substantial utility for using the claimed nucleic acid molecules as a probe for hybridization or as a primer in PCR amplification, the specification does not enable the full breadth of the claims for

using the claimed invention in these manners, even if such use is only in the context of further scientific investigation of the claimed invention.

Footnote 29 suggests several utilities which were not addressed. Contrary to Appellants assertion, the detection of polymorphisms does involve hybridization between either probes or primers with a target nucleic acid (see specification, pages 28-35). With respect to antisense molecules, the issue of how to make and use them is inseparable from the reasons this use has no disclosed patentable utility. In any event, antisense molecules do act by hybridizing to their target mRNA. With respect to transforming cells with the claimed nucleic acids or to raising antibodies, these utilities are directed to making and using, respectively, protein corresponding to the claimed nucleic acid molecules, *not* to the claimed nucleic acid molecules themselves. However, these utilities do require using the claimed nucleic acid molecules as hybridization probes, i.e. as an intermediate, in order to first isolate any corresponding nucleic acids that encode a corresponding protein (specification, page 12, para. 3). The specification does not teach any protein, nor any patentable utility for the protein, either as an end product or as an intermediate. The omission of these utilities from the enablement rejection is of no moment because the brief (at page 9, 2nd full para.) states:

> It is irrelevant whether the corresponding mRNA or polypeptide themselves have utility because Applicants are not relying on utility of the mRNA or polypeptide to establish utility of the claimed nucleic acid molecules.

However, the claimed nucleic acid molecules do embrace any corresponding mRNAs, and any complete cDNA copies thereof, since the disclosed EST is presumed to be a

subsequence contained in these nucleic acids, and may embrace the corresponding genes or chromosomal DNA. The specification does not disclose whether SEQ ID NO: 1 is present in the corresponding gene or chromosomal DNA. For example, if SEQ ID NO: 1 contains a poly(A) sequence added during transcription, or is interrupted by an intron in the chromosomal DNA, then claims 1 and 3 would not embrace the corresponding gene or chromosomal DNA.

To summarize the additional grounds of rejection, the scope of claims 1 and 3 is astronomically huge, when one only considers additional nucleic acid sequences added to SEQ ID NO: 1. While the claims do embrace nucleic acid molecules with predictable hybridization performance characteristics under certain well-controlled conditions, whether as a probe or a primer, the claims are not limited to such nucleic acid molecules, nor do the claims include any functional limitations or intended use limitations restricting their utility to one involving hybridization, or any other function. As pointed out by Appellant, the specification does disclose intended uses (not deemed to meet the utility requirement) that do not involve hybridization, e.g. production of the corresponding protein. The claims embrace many embodiments that would simply not function appropriately in hybridization (no hybridization or hybridization to non-target nucleic acid molecules), and the specification does not teach how to use the large number of embodiments that are inoperative for hybridization. This is not simply a situation where the claims embrace few inoperative embodiments (relative to the scope of the claim) in one disclosed use, e.g. hybridization.

For example, the Wiegand Declaration (at para. 13) states that one skilled in the art would know that addition of soybean sequences to SEQ ID NO: 1 would prevent efficient use of such a combined sequence as a hybridization probe for soybean nucleic acid molecules. However, this presupposes that one would know *a priori* whether any arbitrarily chosen nucleic acid sequence was or was not soybean nucleic acid or would or would not cross-hybridize with other soybean nucleic acid molecules. Such nucleic acid molecules are embraced by the claims.

The Examiner agrees with Appellants that the claims may include inoperative embodiments; however, only if the operative embodiments can be identified without resort to undue experimentation, and the claimed subject matter bears a reasonable correspondence with the enabled embodiments. See e.g. *In re Vaeck*, 20 USPQ2d 1438, 1444-1445, where the affirmance of the rejection of the broad claims was largely due to unpredictability. In *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 224 USPQ 409, 414 (CA FC 1984), the court qualified the statement:

> Even if some of the claimed combinations were inoperative, the claims are not necessarily invalid. "It is not a function of the claims to specifically exclude * * * possible inoperative substances * * * *"

with the statement:

> Of course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid.

It is the latter situation at issue here.

The Examiner agrees with Appellant that lack of absolute predictability does not preclude enablement or that the requirement for " some experimentation ... does not preclude enablement", but holds that the wholesale "make-and test" experimentation

required here to enable the full scope of the claims was not what the courts had in mind. In *Atlas Powder*, the specification in question contained ample guidance for the substituents in the claimed combinations. In contrast, the instant specification contains little guidance on the nature of additional sequences that might be attached to the sequence of SEQ ID NO: 1 for use in hybridization or any other methodology. It is acknowledged that those of skill in the art were aware of various nucleic acids that could be conventionally attached to a probe without adversely affecting its performance characteristics in hybridization, such as a vector backbone or oligonucleotides such as linkers, adapters, or PCR heels (see Wiegand Declaration at para. 13). However, the claims are not limited to nucleic acid molecules further comprising such nucleic acids. The claims embrace adding to SEQ ID NO: 1 any additional nucleic acid, of any length or sequence, regardless of purpose. Adding nucleic acids of arbitrary length and sequence to a probe sequence, such as SEQ ID NO: 1, is *not* conventional in the art. There must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed, see *Vaeck* at page 1445. The specification does not teach which unconventional additional sequences would be consonant with using the claimed nucleic acid molecules in hybridization, nor does it teach how to use those claimed nucleic acid molecules that are unsuitable for hybridization.

The relevance of the "benzpyran" example (brief, page 30), which appears to be hypothetical, to the instant case is unclear. Nucleic acid molecules are not analogous to many types of product, such as benzpyrans. Those in the art employ nucleic acid molecules for many different uses, and these molecules are in heteropolymeric chains of a wide variety of different residue sequences and sizes, from oligonucleotides a few residues in length up to chromosomes of 1,000,000 or more residues in length. Not all

of these are suitable for uses requiring hybridization, nor would those skilled in the art even consider doing so.

Although the level of skill in the hybridization art is high and that the prior art provides ample general guidance on hybridization, the art also recognizes that choosing specific probes for a specific application must be taken on a case by case basis. The only explicit guidance in the specification with regard to a probe is SEQ ID NO: 1 itself. The only generally disclosed target nucleic acids disclosed are SEQ ID NO: 1 and the corresponding mRNA and genomic DNA from soybean and perhaps from other plants. Given this limited disclosure, it is unclear how one skilled in the art would use the vast majority of nucleic acid molecules embraced by the claims, which includes a nucleic acid molecule comprising SEQ ID NO: 1, 469 nucleotides long, attached to 1,000,000 nucleotides, or greatly more, of arbitrary sequence.

Appellants urge (brief, page 31) the concerns that the claims embrace inoperative embodiments "are irrelevant", citing *Atlas Powders* and *Ex parte Cole*, 223 USPQ 94, 95 (BPAI 1983) as support. However, *Atlas Powders* stated that if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid. *Cole* is inapposite because the instant rejection is not based upon any argument that each embodiment be useful for each and every use. Only one use, hybridization, is at issue since the specification does not disclose any other use that does not require hybridization at some point. Furthermore, the claims in *Cole* each contained functional limitations or intended use limitations in addition to structural limitations. The instant claims have no functional or intended use limitations. Pages 31-36 of the brief summarize pertinent case law with respect to enablement and prior art references which show the state of the prior art and the skill of one in the pertinent art. Since the

only working example shows using a claimed nucleic acid molecule, a *conventional* plasmid clone, as a template for PCR amplification, the second and third *Wands* factors do not appear to be met in this case. What is missing from the specification, and the general knowledge in the art, is guidance on the nature of additional nucleic acid added to SEQ ID NO: 1 for uses requiring hybridization. While it is true that a considerable amount of experimentation is permissible if it is routine, i.e. typically performed by those in the pertinent art, that is not the situation here. The issue is not whether it is routine to try different hybridization protocols in order to optimize (see Wiegand Declaration, para. 11). The question is whether it is routine in the art to add arbitrary nucleic acid, of any length or sequence, to a defined probe sequence, e.g. nucleic acid molecule consisting of SEQ ID NO: 1, and whether it is routine to then test such complex probes for operability. The sheer magnitude of the embodiments claimed, i.e. infinite, is evidence that such an undertaking would be extremely laborious and lengthy. The problem here is that the claims embrace far more than would be conventionally employed for uses requiring hybridization. The Court in *Atlas Powders* stated that "if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid". That is the situation here."

Response to Section III. of Applicant's reply

Applicant's arguments boil down to asserting that because a nucleic acid molecule consisting of SEQ ID NO: 1 (or its complete complement) was adequately described, then a genus of nucleic acid molecules comprising SEQ ID NO: 1 was adequately described because the required presence of SEQ ID NO: 1 would distinguish claimed nucleic acid molecules from

nucleic acid molecules not being claimed, and that to hold otherwise mean that every comprising claim ever written would be invalid.

However, the written description requirement is not only to insure that the claimed subject matter can be distinguished from subject matter that is not claimed. It is also to insure that applicant was in possession of the claimed invention as a whole, and that the specification adequately describe the invention as a whole to the public. It is acknowledged above, that a specification need not describe conventional additions to SEQ ID NO: 1 consistent with its disclosed uses in order to adequately describe those embodiments of the claimed nucleic acid molecule, or describe every nuance of the claimed nucleic acid molecules. However, such embodiments make up only a small fraction of embodiments embraced by the claims. The specification discloses that the invention includes, but does not describe in any meaningful way, embodiments wherein the nucleic acid molecule contains additional nucleotides linked to SEQ ID NO: 1 in soybean nucleic acid. Consider, that if one were to randomly add one of the four naturally occurring ribonucleotides to SEQ ID NO: 1, there would be only a 25% probability that a soybean mRNA comprising SEQ ID NO: 1 would also contain that nucleotide at that location. With each successive nucleotide added at random, the probability that this soybean mRNA also contains those nucleotides at the same corresponding positions decreases exponentially. Clearly, one of skill in the art could not have envisioned subsequences of the soybean mRNA that comprised additional nucleotides other than those disclosed for SEQ ID NO: 1. The specification also discloses that the invention includes, but does not describe in any meaningful way, embodiments wherein a nucleic acid molecule comprising SEQ ID NO: 1 encodes the protein of the soybean gene corresponding to SEQ ID NO: 1. The instant

specification provides no evidence that Applicant possessed these embodiments embraced by the claims, and the specification clearly fails to adequately describe them. Yet when the claims are read in light of the specification, they are explicitly included in the claimed invention, e.g., nucleic acid molecules that encode the soybean protein encoded by the gene corresponding to SEQ ID NO: 1.

Applicant asserts (pages 15-16) that additions to SEQ ID NO: 1 are described in the specification at pages 47-54, relating to vectors and page 21, relating to fusion nucleic acid molecules. However, these sections of the specification relate to claimed nucleic acid molecules that encode proteins, and the specification does not describe such proteins beyond alluding to their expected existence. Pages 66-67 relate to the construction of a cDNA library, which is not disclosed as containing any nucleic acid molecule embraced by the claims. The amendment to the specification relating to the deposited clone is new matter for the reasons set forth in the objection to the specification, and cannot support Applicant's arguments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310 (after 1/12/04 – (571) 272-0733). The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

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